Approved for use through 07/31/2006, OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

der the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless I ti contains a valid OMB control number.

for form 1449/PTO

A RAMAN

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known				
Application Number	09/214,371			
Filing Date	March 26, 1999			
First Named Inventor	David P. Lane			
Art Unit	1635			
Examiner Name	Zara, Jane J.			
Attorney Docket Number	39749-0002 US			

Sheet 1 of 5

U.S. PATENT DOCUMENTS

*Examiner Initials		Cite No.	5000		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	3	A1	US	5,411,860	05-02-1995	Vogelstein et al.	·
	0	A2	us	5,519,118	05-21-1996	Vogelstein et al.	
		А3	US	5,532,348	07-02-1996	Huibregtse et al.	
		A4	US	5,550,023	08-27-1996	Kinzler et al.	
		A5	US	5,606,044	02-25-1997	Burrell et al.	
	V	A6	us	5,618,921	04-08-1997	Burrell et al.	

	FOREIGN PATENT DOCUMENTS							
			Foreign Patent Document	Publication		Pages, Columns, Lines, Where Relevant		
*Examiner Initials		No.	County Code ³ -Number ⁴ -Kind Code ⁵ (if known)	Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Passages or Relevant Figures Appear		
S.	5	-B1	PCT WO 94/00601	01-06-1994	Levine et al.			
7		B2	PCT WO 94/08241	04-14-1994	Zentgraf et al.	NOTransla.		
		В3_	PGT WO 94/10306	05-11-1994	Soussi et al.	No Transa.		
	Π	B4	PCT WO 98/01467	01-15-1998	Lane et al.			
\ \		B5	PCT WO 98/13064	04-02-1998	Lu et al.			

EXAMINER SIGNATURE

DATE CONSIDERED

5/24/05

*EXAMINER: Initial if reference considered, whether or dot citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached. This collection is information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing his burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
rademark Office; U.S. DEPARTMENT OF COMMERCE

Substitute (a form 1449/PTO INFORMATION DISCLOSURE			TO		Comp	olete if Known	
			ISCLOSURE	Application Number	09/214,371		
	STATEMENT BY APPLICANT (use as many sheets as necessary)				Filing Date	3/26/1999	
					First Named Inventor	David P. Lane	
				•	Art Unit	1635	
					Examiner Name	Zara, Jane J.	
				·	Attorney Docket Number	39749-0002 US	
Sheet		2	of	5			•
		OTI	IFR D	OCUMENTS - NO	N-PATENT LITERATURE	DOCUMENTS	
*Examiner Initiats	Cite No.1		nclude na	me of the author (in CAPITA	L LETTERS), title of the article (when a al, symposium, catalog, etc.), date, pag ther, city and/or country where published	ppropriate), title of the e(s), volume-issue	т²
$\overline{\bigcap_{i}}$	C1	Barak, Y 468, Feb	-	"mdm2 expression is in	nduced by wild type p53 activity	," EMBO J., 12(2): 461-	
GO	C2	Barak Y	& Oren		g of a 95 kDa protein to p53 in c (6): 2115-2121, Jun 1992	ells undergoing p53-	
	C3	Böttger /	A. et al.		: Mdm2-binding mini protein tha	t activates the p53	
	C4	Brown D	R. et a	I., "The tumor suppres	sor p53 and the oncoprotein simom protein," Mol. Cell. Biol., 13	nian virus 4D T antigen 8(11): 6849-6857, Nov	
	C5	Cahilly-S	from a		alysis and chromosomal mappin 3 cell line," Somatic Cell Mol. G		
	C6			., "Interactions between S USA, 91(7): 2684-268	n p53 and MDM2 in a mammalia 88. Mar 1994	an cell cycle checkpoint	
	C7	Chen J. 4114, Ju	et al., "	Mapping of the p53 and	d mdm-2 interaction domains," N	Mol. Cell Biol., 13: 4107-	
	C8	Colas P.	et al., '	'Genetic selection of pesse 2," Nature, 380: 548	eptide aptamers that recognize	and inhibit cyclin-	
	C9		et al.,	The tumor suppressor	p53 regulates its own transcrip	tion," Mol. Cell. Biol., 13:	
	C10	Dyson N	. et al.,	"Adenovirus E1A make 4606-4611, Jul 1992	es two distinct contacts with the	retinoblastoma protein,"	
	C11	Dyson N proteins Dec 199	l. <i>et al.</i> , mediat 2	"Homologus sequence e interaction with the sa	es in adenovirus E1A and huma ame set of cellular proteins," J. \	Virology, 66: 6893-6902,	
	C12	Farmer (G. et al.	, "Wild-type p53 activa	tes transcription in vitro," Nature	e, 358: 83-86, Jul 1992	

DATE CONSIDERED

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

EXAMINER SIGNATURE

^{*}EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S. C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

Commissioner for Patents. P.O. Box 1450, Alexandria, VA 22313-1450. Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03)

Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

The Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless It I contains a valid OMB control number.

(5)	Substitute of form 1449/PTO
	INFORMATION DISCLOSURE
	STATEMENT BY APPLICANT

(use as many sheets as necessary)

Comp	plete if Known
Application Number	09/214,371
Filing Date	3/26/1999
First Named Inventor	David P. Lane
Art Unit	1635
Examiner Name	Zara, Jane J.
Attorney Docket Number	39749-0002 US

of Sheet

		OTHER DOCUMENTS - NON-PATENT LITERATURE DOCUMENTS	
*Examine Initials	r Cite	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	Т²
172) C13	Finlay, C.A., "The mdm-2 Oncogene can overcome wild-type p53 suppression of transformed cell growth," Mol. Cell. Biol., 13(1): 301-306, Jan 1993	
14	C14	Florenes V.A. et al., "MDM2 gene amplification and transcript levels in human sarcomas: Relationship to TP53 gene status," J. Nat. Cancer Institute, 86(17): 1297-1302, Sep 1994	
·	C15	Funk W. D. et al., "A transcriptionally active DNA-binding site for human p53 protein complexes," Mol. Cell. Biol., 12(6): 2866-2871, Jun 1992	
	C16	Garcia-Echeverria C. et al., "Structure activity studies of peptide inhibitors of the p53-HDM2 interaction," 15 th American Peptide Symposium, Jan 1997	
	C17	Haupt Y. et al., "Cell type-specific inhibition of p53-mediated apoptosis by mdm2," EMBO J., 15(7): 1596-1606, Apr 1996	
	C18	Hupp T.R. et al., "Small peptides activate the latent sequence-specific DNA binding function of p53," Cell, 83: 237-245, Oct 1995	
	C19	Jones S.N. et al., "Rescue of embryonic lethality in Mdm-1deficient mice by absence of p53," Nature, 378: 206-208, Nov 1995	
	C20	Juven T. et al., "Wild type p53 can mediate sequence-specific transactivation of an internal promoter within the mdm2 gene," Oncogene, 8(12): 3411-3416, Dec 1993	
П	C21	Kern S.E. et al., "Oncogenic forms of p53 inhibit p53-regulated gene expression," Science, 256: 827-830, May 1992	
	C22	Kovar H. et al., "Narrow spectrum of infrequent p53 mutations and absence of MDM2 amplification in Ewing tumours," Oncogene, 8(10): 2683-90, Oct 1993	
	C23	Kussie P.H. et al., "Structure of the MDM2 oncoprotein bound to the p53 tumor suppressor transactivation domain," Science, 274: 948-953, Nov 1996	
\prod	C24	LaVallie E.R. et al., "A thioredoxin gene fusion expression system the E. coli cytoplasm," Biotechnology, 11(2): 187-193, Feb 1993	
1	C25	Lane D. et al., "On the regulation of the p53 tumour suppressor, and its role in the cellular response to DNA damage," Phil. Trans. R. Soc. Lond. B, 347: 83-87, 1995	

EXAMINER SIGNATURE

DATE CONSIDERED

^{*}EXAMINER: Initial if reference considered, whether or dot citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation frumber (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S. C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/08B (08-03)

Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE nder the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless It I contains a valid OMB control number.

or form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Complete if Known				
Application Number	09/214,371			
Filing Date	3/26/1999			
First Named Inventor	David P. Lane			
Art Unit	1635			
Examiner Name	Zara, Jane J.			
Attorney Docket Number	39749-0002 US			

Sheet of

		OTHER DOCUMENTS - NON-PATENT LITERATURE DOCUMENTS	
"Examiner Initials	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	۲² .
72	Lees-Miller S.P. et al., "Human DNA-activated protein kinase phosphorylates serines 15 and 37 in the amino-terminal transactivation domain of human p53," Mol. Cell Biol., 12(11):5041-5049, Nov 1992		
10	C27	Lin J. et al., "Functions of the p53 protein in growth regulation and tumor suppression," Cold Spring Harbor Symposia on Qualitative Biology, LIX: 215-223, 1994	
	C28	Lin Y & Green M., "Similarities between prokaryotic and eukaryotic cyclic AMP-responsive promoter elements," Nature, 340: 656-659, Aug 1989	
	C29	Liu X. et al., "The p53 activation domain binds the TATA box-binding polypeptide in holo-TFIID, and a neighboring p53 domain inhibits transcription," Mol. Cell. Biol., 13: 3291-3300, Jun 1993	
	C30	Lu X. & Lane D., "Differential induction of transcriptionally active p53 following UV or □onizing radiation: Defects in chromosome instability syndromes?," Cell, 75: 765-778, Nov 1993	
	C31	Martin K. et al., "Stimulation of E2F1/DP1 transcriptional activity by MDM2 oncoprotein," Nature, 375: 691-698, Jun 1995	
	C32	Marston N.J. et al., "Interaction of p53 with MDM2 is independent of E6 and does not mediate wild type transformation suppressor function," Oncogene, 9: 2707-2716, Sep 1994	
	C33	Michalovita D. et al., "Conditional inhibition of transformation and of cell proliferation by q temperature-sensitive mutant of p53," Cell, 62: 671-680, Aug 1990	-
	C34	Midgley C.A. et al., "Analysis of p53 expression in human tumours: an antibody raised against human p53 expressed in Escherichia coli," J. Cell Science, 101(1): 183-189, Jan 1992	
	C35	Montes de Oca Luna R. et al., "Rescue of early embryonic lethality in mdm1-deficient," Nature, 378: 203-206, Nov 1995	
	C36	Oliner J.D. et al., "Amplification of a gene encoding a p53-associated protein in human sarcomas," Nature, 358: 80-83, Jul 1992.	
J	C37	Oliner J.D. et al., "Oncoprotein MDM1 conceals the activation domain of tumour suppressor p53," Nature, 262: 857-860, Apr 1993	

EXAMINER SIGNATURE

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformatic and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S. C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450. Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

PTO/SB/088 (08-03) Approved for use through 07/31/2006. OMB 0651-0031 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Inder the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless It i contains a valid OMB control number.

for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Сот	plete if Known
Application Number	09/214,371
Filing Date	3/26/1999
First Named Inventor	David P. Lane
Art Unit	1635
Examiner Name	Zara, Jane J.
Attorney Docket Number	39749-0002 US

5 of Sheet

July 1993

EXAMINER SIGNATURE

		OTHER DOCUMENTS - NON-PATENT LITERATURE DOCUMENTS									
	Exan Initiati		Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T²						
$\sqrt{2}$		2	C38	Otto A. & Deppert W, "Upregulation of mdm-2 expression in meth a tumor cells tolerating wild-type p53," Oncogene, 8(9): 2591-2603, Sep 1993							
1		0	C39 ,	Picksley S. & Lane D., "The p53-mdm2 autoregulatory feedback loop: a paradigm for the regulation of growth control by p53," BioEssays, 15(10): 689-699, Oct 1993							
			C40	Renzing J. & Lane D., "p53-dependent growth arrest following calcium phosphate-mediated transfection of murine fibroblasts," Oncogene, 10(9): 1865-1868, May 1995							
			C41	Schlaeppi JM. et al., "Identification of specific hdm2 binding peptides by affinity selection and mass spectrometry," 17 th International Congress of Biochemistry and Molecular Biology, San Francisco, USA, Aug 1997							
			C42	Schlichtholz B. et al., "The immune response to p53 in breast cancer patients is directed against immunodominant epitopes unrelated to the mutational hot spot," Cancer Res., 52: 6380-6384, Nov 1992							
			C43	Stephen C.W. et al., "Characterisation of epitopes on human p53 using phage displayed peptide libraries: Insights into antibody-peptide interactions," J. Mol. Biol., 248(1): 58-78, Apr 1995							
			C44	Unger T. et al., "P53: a transdominant regulator of transcription whose function is ablated my mutations occurring in human cancer," EMBO J., 11(4): 1383-1390, Apr 1992							
			C45	Vojtesek B. & Lane D., "Regulation of p53 protein expression in human breast cancer cell lines," J. Cell Science, 105(3): 607-612, Jul 1993							
			C46	Wasylyk C. et al., "P53 mediated death of cells overexpressing MDM2 by an inhibitor of MDM2 interaction with p53," Oncogene 18: 1921-1934, Mar 1999							
•		$\neg \neg$									

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered.

Wu X. et al., "The p53-mdm-2 autoregulatory feedback loop," Genes & Dev., 7: 1126-1132,

DATE CONSIDERED

Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation humber (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S. C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.